

**b.) Remarks**

Claims 2, 3 and 17 have been amended in order to recite the present invention with the specificity required by statute. Additionally, Claims 4-8, 18 and 23-24 are amended for better conformity with their antecedent claims or for better idiomatic usage. Claims 1, 9-15, 19-22 and 25-28 are cancelled in order to reduce the issues. No new matter has been added.

Claims 1-28 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In response, the claims have been amended in order to address each of the Examiner's noted concerns.

Claims 20-22 and 26-28 are rejected as being "use" claims and under 35 U.S.C. §101 as not reciting steps. As noted, these claims have above been cancelled.

Claims 17 and 23 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In response, these claims have been amended to specify treating a solid tumor, in conformity with Test Example 1.

Claims 9-11 and claims 12-15 are objected to under 37 C.F.R. §1.75 as being a substantial duplicate of claims 1 and 2-5, respectively. Again, as noted, these claims have been cancelled.

Claims 1-3 are rejected under 35 U.S.C. §102(a) as being anticipated by Schupp et al. (J. Natural Products (1999), 62(7), 959-962), and under 35 U.S.C. § 102(b) as anticipated by Yamada et al. (J. Antibiotics (1996) 49(10) 1070-1072, Murakata et al. (U.S. Patent No. 5,604,219), Tamaoki (U.S. Patent No. 5,674,867), Yamada et al. (JP 5140168), Tsubotani et al. (Tetrahedron (1991), 47(22), 3565-74) and "Yamada et al." (sic, Tanida) (JP 01149791).

As to Schupp, claim 1 was cancelled and claims 2 and 3 were amended to distinguish RN 23978-04-7P and 239785-05-8P, at least, by the substituent on 3-position (corresponding to  $R^{1A}$  and  $R^{1B}$ ). For the same reason, claims 2 and 3 can not read on the cited compounds in Yamada (Journal of Antibiotics (1996), 49(10), 1070-1072), Yamada (JP 5140168), Tsubotani (Tetrahedron (1991), 47(22), 3565-74) and Tanida (JP 01149791).

In Murakata (US 5,604,219), the substituent on 2-position (corresponding to  $NH$  of lactam in the formula (IA) and (IB)) is substituted or unsubstituted lower alkyl. Claims 2 and 3 do not read on any of the compounds in Murakata Table 1, cols. 13-16.

In Tamaoki (US 5,674,867), the 5- and 17- position substituents are hydrogen, hydroxy, lower alkoxy, lower alkanoyl and halogen. However, the combinations of substituents on 5- and 17-positions of claim 2 ( $R^{2A}$  and  $R^{3A}$ ) and claim 3 ( $R^{3B}$  and  $R^{2B}$ ) are not taught by the reference.

Claims 1-3 are rejected under 35 U.S.C. §103(a) as being unpatentable over Cantrell et al. (Natural Product Letters (1999), 14(1), 39-46) or Funato et al. (Tetrahedron Letters (1994), 35(8), 1251-4). In general, in support of the rejection, the Examiner states that the claims variously differ by requiring the substituent on the benzene rings at an adjacent position, or by being structurally obvious ring position isomers.

As to claims 2 and 3, the substituents on 3- position ( $R^{1A}$  or  $R^{1B}$ ) in formula (IA) and (IB) represent hydroxy or lower alkoxy ( $R^{1A}$  and  $R^{1B}$  are not hydrogen). In contrast, Cantrell and Funato teach compounds wherein the substituents corresponding to  $R^{1A}$  and  $R^{1B}$  represent hydrogen.

These are not insignificant changes. Aside from (1) there being no teaching or suggestion in the prior art for making these particular modifications at those particular positions, (2) it is well-known that hydroxy and alkoxy groups drastically affect the


physical properties of the compounds.<sup>1/</sup> Furthermore, (3) it is also well-known that the oxygen atom in hydroxy and alkoxy groups is a proton acceptor for a hydrogen bond formation. Since these hydrogen bonds form between the compound and the target, compound activities tend to vary in kind.

In view of the above amendments and remarks, Applicants submit that all of the Examiner's concerns are now overcome and the claims are now in allowable condition. Accordingly, reconsideration and allowance of this application is earnestly solicited.

Claims 2-8, 16-18 and 23-24 remain presented for continued prosecution.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,

  
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<sup>1/</sup> Such as solubility, polarity, lipophilicity and, when appropriate, melting point.